Research Journal of Environmental Toxicology

ISSN 1819-3420

Academic Journals Inc.

www.academicjournals.com

OPEN ACCESS Research Journal of Environmental Toxicology

ISSN 1819-3420
DOI: 10.3923/rjet.2024.1.7

Research Article
Assessment of the Acute Toxicity of "Oxamax®", Carbamate Insecticide Based Oxamyl (50 mg/kg)

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Abstract

Background and Objective: Carbamate pesticides are recognized for their high acute toxicity with an inhibitory action on acetylcholinesterase activity. This study aims to evaluate the acute toxicity of "Oxamax®", a carbamate insecticide, an oxamyl-based formulation, in rats and rabbits. **Materials and Methods:** Oncins France Strain A (OFA) rats aged 8 to 12 weeks were used for acute oral and respiratory toxicity tests. For skin and eye toxicity tests, rabbits of the New Zealand breed with an average weight of 3 kg were used. The various tests were conducted according to OECD guidelines for chemical testing. Acetylcholinesterase activity was assessed in animals exposed to the respiratory route. **Results:** Animals treated orally showed clinical signs of toxicity (apathy, drowsiness, convulsions and death) at a dose of 300 mg/kg. With an oral Lethal Dose 50 (LD_{50}) in rats between 50 and 300 mg/kg, Oxamax® can be classified in category 3 of the Globally Harmonised System of Classification and Labelling of Chemicals (GHS). The primary dermal irritation index (PDII) determined for this carbamate is 3.11. Oxamax® is classified as moderately irritating to the skin. The maximum mean total score (MMTS) for "Oxamax®" was 46.3, classifying the product as moderately irritating to the eyes. The rate of inhibition of cholinesterase activity varied from 23.9 to 83.17% for doses ranging from 0.5 to 5 mg/L following exposure for 4 hrs. **Conclusion:** Like most carbamate pesticides, "Oxamax®" exerted high acute toxicity by the oral, dermal, ocular and respiratory routes. This molecule must be used in strict compliance with the instructions for use.

Key words: Carbamate, Oxamax®, oxamyl, acute toxicity, acetylcholinesterase

Citation: Manda, P., A.J.B. Adepo and J.V. N'gbe, 2024. Assessment of the acute toxicity of "Oxamax®", carbamate insecticide based oxamyl (50 mg/kg). Res. J. Environ. Toxicol., 18: 1-7.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Pesticides are a group of chemical substances used to combat harmful and undesirable species. These agro-pharmaceutical products are used in agriculture for crop protection and in community health for vector control. Certain chemical families of pesticides such as carbamates and organophosphates have been widely used in recent decades due to their low accumulation in the environment[1,2]. Carbamates act on a very large number of insects, in particular aphids, mites and nematodes, on which they exert high acute toxicity due to their cholinesterase-inhibiting action[3,4]. Poisoning by carbamate pesticides is of variable intensity and linked to the nature and dosage of the active ingredient[5]. In humans and various non-target animal species, carbamate acute toxicity is characterized by a muscarinic syndrome often associated with neuropathy in the days and weeks following exposure[6,7]. Several studies estimate that 220,000 to 300,000 people die each year in the world as a result of poisoning by pesticides, 99% of which come from developing countries[8-10]. In Côte d'Ivoire, occupational poisoning linked to carbamate and organophosphates pesticides has been reported by several studies[11,12]. Because of their highly toxic nature, the synthesis, sale and use of pesticides are preceded by toxicological studies making it possible to set regulatory standards in humans, in foodstuffs and environmental matrices. Compliance with established standards leads to the safe use and management of pesticides. Oxamyl is a carbamate that is marketed in various forms[13].

In granular form, this molecule is subject to restrictions on use due to its high acute toxicity for humans and animals in the event of exposure by the oral, dermal and respiratory routes[14]. Several carbamates of varying toxicity have been formulated using oxamyl as the active substance. This is the case with Oxamax®, a formulation containing 50 mg/kg of oxamyl, which is used as a nematicide in cotton cultivation. In this formulation, Oxamax® has not been the subject of any studies concerning its possible toxic effects on either humans or the environment. The aim of this study was therefore to obtain a toxicological file on this pesticide with a view to its registration and marketing. The aim was to assess the acute toxicity of Oxamax® by local (skin, eye) and systemic (oral, respiratory) routes.

MATERIALS AND METHODS

Study area: This study was carried out from March 3 to May 5, 2022 at the Laboratory of Toxicology of the Research-Training Unit of Pharmaceutical and Biological Sciences, University Felix Houphouët Boigny, Abidjan.

Insecticide sample: The product to be tested is called "Oxamax®". It is presented in the form of dry granules, light green in color. The active ingredient of "Oxamax®" is oxamyl dosed at 50 g/kg. Its crude formula is $C_7H_{13}N_3O_3S$. The samples of "Oxamax®" were provided to us by the company responsible for the formulation and marketing of this pesticide.

Biological material: Two animal species were used for this study. Forty Oncins France Strain A (OFA) rats were purchased from the animal store of the Félix Houphouët Boigny University of Abidjan. The age of the rats varies between 8 and 10 weeks with an average weight of 190 g. Eight albino rabbits of New Zealand breed with an average weight of 3 kg were purchased from a breeding farm in the suburbs of Abidjan. The treated animals were acclimatized to laboratory conditions for 7 days before the various experiments.

Methods

Acute toxicity study

Acute oral toxicity study: The test was conducted according to the OECD 423 guideline[15]. Three dose levels (5, 50 and 300 mg/kg) were tested following a sequential procedure. In total, 18 rats divided into 3 groups of 6 rats were treated with "Oxamax®". The animals were fasted for 16 hrs then weighed and the test substance was administered by gavage at the rate of 1 mL per 100 g of body weight. The test was repeated twice. The treated animals were observed for 14 days in search of possible signs of acute intoxication. Observations focused on changes in the skin, hair, eyes and mucous membranes, as well as changes affecting the respiratory system, circulatory system, autonomic and central nervous system and somatomotor activity.

Primary skin irritation test: This study was conducted by application of the OECD 404 guideline[16]. Three albino rabbits were used for the experiment. The test sample was applied to the shaved right flank (an area of approximately 6 cm^2) of the skin and covered with a gauze pad, secured with a non-irritating plaster. The shaved left flank served as a control. The initial test was carried out on a single animal and then confirmed on two other animals. Observations are made on the treated area compared to the control area according to the product classification table and their index. The primary irritant effect on the skin corresponds to the reversible

inflammatory phenomena following the application of the substance to be treated to the skin for 4 hrs. The observation of skin lesions (erythema and edema) was scored according to the Draize dermal irritation scoring system[17]. The primary dermal irritation index (PDII) was calculated using the following formula[18]. The PDII allowed to classify the tested product according to the Draize method of classification:

$$PDII = \frac{\sum \text{Erythema at } 24/48/72 \text{ hrs} + \sum \text{Oedema at } 24/48/72 \text{ hrs}}{3 \times \text{number of animals}}$$

Determination of eye irritation index: This study in rabbits was carried out according to the OECD 405 guideline[19]. The test was carried out by introducing 0.1 g of the test substance into the conjunctival sac of the right eye of the rabbit, after separating the lower eyelid from the eyeball. The untreated left eye served as a control. Animals were observed at 4, 24, 48 and 72 hrs after installation of "Oxamax®" for acute distress and/or pain. Observation of signs of animal distress was rated according to the Draize eye irritation scoring system[20]. The toxicity of the test substance was classified according to the highest mean score (maximum mean total score (MMTS)).

Study of acute toxicity by the respiratory route: The acute inhalation toxicity study was performed according to the OECD 436 guideline[21]. The "nose only" exposure to aerosol vapors was chosen for this study. Three dose levels were tested: 0.5, 1 and 5 mg/kg. For each step, 6 animals were used. A total of 18 rats were treated with "Oxamax®" in 3 groups of 6 rats. The exposure time of the animals was 4 hrs. The test was repeated twice. Clinical examination of the animals was performed regularly during and after exposure over a period of 14 days. Daily observations included changes in skin and hair, eyes and mucous membranes, as well as changes in the respiratory system, circulatory system, autonomic and central nervous systems, somato-motor activity and behavior.

Serum cholinesterase test: Blood was collected from the orbital vein in rats with respiratory exposure for serum cholinesterase determination. The decrease in cholinesterase activity allows us to confirm the diagnosis of intoxication with carbamate compounds. After centrifugation of the collected blood, the serum, separated from the pellet, was used for the determination of serum cholinesterase by the colorimetric method[22].

Histological examinations: Kidney, lung and liver were collected from orally and respiratory exposed animals and these organs were immediately fixed in 10% formalin. The organs were placed in cassettes and then loaded into baskets to be dehydrated with technicon (delay timer, sacora). The samples, deparaffinized, were then stained with hematoxylin and eosin and observed under a light microscope (Optika, Italy).

Statistical analysis: Data were processed using Microsoft Office Excel 2013 software. Data entry, calculation of means and student tests were performed using this software.

RESULTS

Acute oral toxicity study

Weight evolution of the animals: Body weight gains during the 14 days (D14) of observation were 13.83, 11.89 and 10.16 g for animals in the control group 1 and 2, respectively (Table 1). There was no significant difference between the body weights of animals in group 2 and 3 compared to animals in the control group. In group 3 (300 mg/kg), all animals died 30 min after administration.

Clinical signs of intoxication: The clinical signs observed for animals in group 1 and 2 were apathy, drowsiness and convulsion. At the dose of 300 mg/kg, all animals died half an hour after administration following violent convulsions. The oral Lethal Dose 50 (LD_{50}) of "Oxamax®" is between 50 and 300 mg/kg.

Primary irritation index: Erythema and oedema have been observed on the surface of the skin treated with Oxamax® (Table 2). The primary irritation index (PDII) of "Oxamax® is equal to 3.11. Oxamax® may be classified as moderately irritating to the skin.

Acute ocular toxicity study: Signs of ocular toxicity are characterized by significant discharge, swelling of the eyelids, chemosis and purple discoloration of the conjunctivitis. The maximum mean total score (MMTS) determined is equal to 46.3, classifying this product as moderately irritating to the eyes (Table 3).

Inhalation toxicity study: After inhalation of "Oxamax®", the clinical signs of intoxication observed include tremors, convulsions, acceleration of respiration and death (Table 4). All animals treated with the 5 mg/kg dose died.

Table 1: Animals average weight variation (g) during the test period (days)

	Average weight of the animals (g)			
Doses administered (mg/kg)	D0	D14	Variation (g)	Student test (5%)
Control group: 0	202.17±50	216±7	+13.83	
Group 1: 5	180.32±48	192.27±27	+11.89	NS
Group 2: 50	186.17±46	196.33±31	+10.16	NS
Group 3: 300	197.67±41	Death	-	-

NS: Not significant

Table 2: Determination of primary irritation index according to Draize scoring system

		Erythema score			Oedema score		
Animal number	Test	24 hrs	48 hrs	72 hrs	24 hrs	48 hrs	72 hrs
1	Initial	3	2	2	3	3	3
2	Confirmatory	2	1	0	2	1	0
3		2	1	0	2	1	0
Total score		7	4	2	7	5	3
Primary dermal irritation index (PDII)				3.11			

Table 3: Assessment of eye irritation according to Draize scoring system

Observation period (hrs)		4 hrs			24 hrs			48 hrs			72 hrs		
Animal number		1	2	3	1	2	3	1	2	3	1	2	3
Cornea	Opacity 0-4 (A)	3	2	2	2	2	1	2	1	0	1	0	0
	Area involve 1-4 (B)	2	2	2	2	1	1	1	1	0	0	0	0
	Score =A×B×5 (max = 80)	30	20	20	20	10	5	10	5	0	0	0	0
Iris	Degree of congestion 0-2 (C)	2	2	1	1	1	1	0	1	0	0	0	0
	Score = C×5 (max = 10)	10	10	5	5	5	5	0	5	0	0	0	0
Conjunctivitis	Chemosis 0-4 (D)	3	2	3	2	1	2	2	1	1	0	1	0
	Discharge 0-3 (E)	3	3	3	3	2	2	1	1	0	0	0	0
	Redness 0-3 (F)	1	2	2	1	1	0	1	0	0	0	0	0
	Score = (D+E+F)×2 (max = 20)	14	14	16	12	8	8	8	4	2	0	2	0
Total score (max = 110)		54	44	41	37	23	18	18	9	2	5	2	0
Mean total score			46.3			26			9.67			3.5	
Maximum mean total score (MMTS)							46.3						

Table 4: Clinical signs of intoxication in exposed rats

		Mortality	
Initial concentration (mg/L)	Signs of intoxication	Number	Time of death (hrs)
0.5	Trembling and bristling hair	0/6	-
1	Trembling, bristling hair, rapid breathing and death	2/6	From 3 hrs15 min of exposure
5	Violent convulsions, abdominal bloating and death	6/6	From 45 min of exposure

Table 5: Degree of cholinesterase inhibition in exposed rats

Dose (mg/kg)	Average cholinesterase levels (UI)	Cholinesterase activity (%)	Degree of enzymatic inhibition (%)
0.5	425.76	76.07	23.90
1	260.66	49.30	50.67
5	94.15	14.01	83.17

Determination of the Lethal Concentration 50 (LC_{50}): The dose of 0.5 mg/L did not cause any mortality among the animals. On the other hand, at a dose of 1 mg/kg, 2 animals died and a dose of 5 mg/L caused the death of all the animals. The LC_{50} can therefore be between 2 and 2.5 mg/L. This means that Oxamax® can be classified in category 4 of the GHS. This carbamate pesticide may be classified in GHS category 4 by the inhalation route.

Determination of cholinesterase activity: The degree of cholinesterase inhibition for the 0.5, 1 and 5 mg/L doses were 23.90, 50.67 and 80.17%, respectively (Table 5). The test sample caused cholinesterase inhibition in a dose-dependent manner.

Histological examinations: Kidneys from rats exposed orally to 300 mg/kg showed a lesion predominantly in the renal

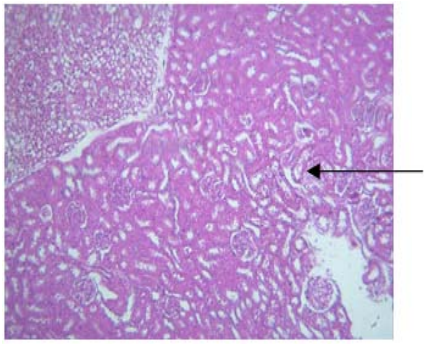

Fig. 1: Photograph of the kidney of rats treated orally with 300 mg/kg showing dilatation with cellular swelling of the glomeruli (black arrow)
H&E stain ×100

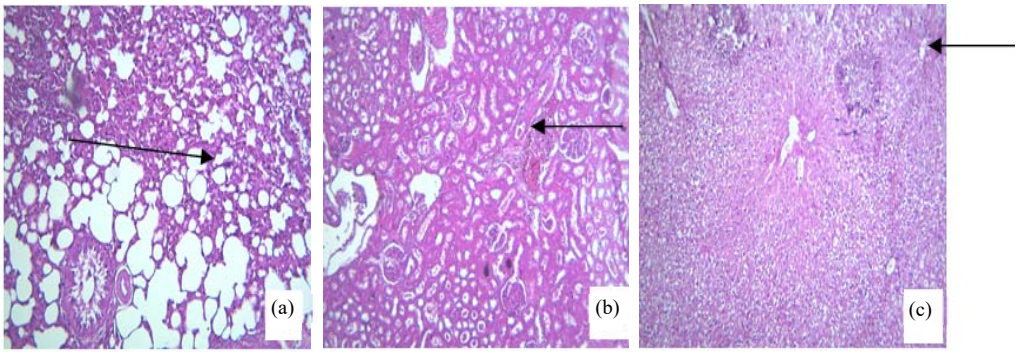

Fig. 2(a-c): Photograph of the organs of rats treated by respiratory route at the dose of 5 mg/L, (a) Lungs showing alveolar-interstitial pneumopathy (arrow), (b) Kidney with tubular necrosis (arrow) and (c) Liver fatty degeneration with inflammatory infiltrate (arrow)
H&E stain ×100

tubules resulting in dilatation with cellular swelling of the glomeruli (Fig. 1). In rats exposed by the inhalation route, histological examinations were performed on the lung, kidney and liver at a dose of 5 mg/L. At this dose, the lungs showed toxicity of the alveolar-interstitial pneumopathy type. In the kidney, tubular necrosis, vascular congestion and infiltrates were observed (Fig. 2). The whole is suggestive of acute renal failure. The liver tissue fragments examined showed fatty degeneration with micro and macro vacuolar steatosis, vascular congestion and inflammatory infiltrate.

DISCUSSION

Carbamates are highly acutely toxic following absorption via the cutaneous, respiratory and oral routes[23,24]. The degree of exposure depends on several factors including the type of formulation, preparation and application techniques and the environment of use[1]. Oral administration of Oxamax® resulted in several intoxications in rats. The main acute clinical signs observed were central nervous system disorders (apathy, somnolence and convulsions) and death. The oral LD_{50} of Oxamax® in rats is between 50 and 300 mg/kg. This carbamate can be classified as a category 3 substance according to the GHS classification. The active ingredient in Oxamax® is oxamyl, whose oral LD_{50} is estimated at between 2.5 and 3.1 mg/kg[25]. The low toxicity of Oxamax® (50 mg/kg) by the oral route is linked to a lower concentration of the active ingredient. The cutaneous and ocular routes are significant absorption routes for carbamates. Because of their lipophilic nature, these compounds easily pass through the dermal and epidermal layers into the general circulation[1,3]. During this experiment, signs of skin irritation such as erythema and oedema were recorded. The primary dermal irritation index of the test substance in rabbits was 3.11. This nematocidal carbamate can be classified as moderately irritating to the skin. Also, animals exposed to the ocular route showed inflammation characterised by heavy tearing with swelling of the eyelids. The maximum mean total score (MMTS) for "Oxamax®" was

46.3 classifying the product as moderately irritating to the eyes. The irritant effects are undoubtedly linked to the intrinsic toxicity of oxamyl, the active substance in "Oxamax®". Like most carbamates, oxamyl is a skin and eye irritant[14]. The Oxamax® formulation is therefore only slightly toxic by the inhalation route, unlike oxamyl (the active substance), which is highly toxic by the same route, with an LC_{50} of between 0.12 and 0.17 mg/L in rats[25]. Carbamates have a reversible inhibitory action on acetylcholinesterase (AChE), an enzyme that hydrolyses acetylcholine, a neurotransmitter involved in cholinergic transmission[3]. In animals exposed via the respiratory route, a dose-dependent decrease in cholinesterase activity was observed. Inhibition rates varied from 23.90 to 83.17% for doses ranging from 0.5 to 5 mg/L. Signs of toxicity in animals exposed by the respiratory route were tremors, accelerated respiratory rate and death. These toxic manifestations could be linked to AChE inhibition. The accumulation of acetylcholine in the synaptic spaces following inhibition of AChE leads to continuous transmission of the nerve impulse responsible for the tremors and accelerated heart rate observed. Histological examinations of various organs (lungs, kidneys, liver) in rats exposed to "Oxamax®" by the respiratory and oral routes revealed toxic effects at doses of 5 mg/L and 300 mg/kg respectively. Local effects included lesions in the pulmonary alveoli. Systemic toxicity was also observed in the liver and kidneys, manifested by disorganisation of the liver parenchyma and renal tubular necrosis. These results are corroborated by several studies that have highlighted the renal, hepatic and pulmonary toxicity of carbamates[7,26].

CONCLUSION

This study highlighted the acute toxicity of Oxamax® via the various possible routes of absorption. This oxamyl-based carbamate showed high toxicity by the oral route, moderate toxicity by the cutaneous and ocular routes and low toxicity by the respiratory route. Like most carbamates, Oxamax® is an acetylcholinesterase inhibitor. In-depth studies on sub-acute and chronic toxicity should be considered to assess the short, medium and long-term effects of this formulation.

REFERENCES

1. Soloneski, S., M. Kujawski, A. Scuto and M.L. Larramendy, 2015. Carbamates: A study on genotoxic, cytotoxic, and apoptotic effects induced in Chinese hamster ovary (CHO-K1) cells. Toxicol. *In vitro*, 29: 834-844.
2. Bhatt, P., X. Zhou, Y. Huang, W. Zhang and S. Chen, 2021. Characterization of the role of esterases in the biodegradation of organophosphate, carbamate, and pyrethroid pesticides. J. Hazard. Mater., Vol. 411. 10.1016/j.jhazmat.2020.125026.
3. King, A.M. and C.K. Aaron, 2015. Organophosphate and carbamate poisoning. Emerg. Med. Clin. North Am., 33: 133-151.
4. Lenina, O.A., I.V. Zueva, V.V. Zobov, V.E. Semenov, P. Masson and K.A. Petrov, 2020. Slow-binding reversible inhibitor of acetylcholinesterase with long-lasting action for prophylaxis of organophosphate poisoning. Sci. Rep., Vol. 10. 10.1038/s41598-020-73822-6.
5. Garcia, F.P., S.Y.C. Ascencio, J.C.G. Oyarzun, A.C. Hernandez and P.V. Alavarado, 2012. Pesticides: Classification, uses and toxicity. Measures of exposure and genotoxic risks. J. Res. Environ. Sci. Toxicol., 1: 279-293.
6. de Oliveira, M.L.F. and A.A. Buriola, 2009. Severity of poisoning by cholinesterase inhibitor insecticides in the Northwest of the State of Paraná, Brazil. Rev. Gaúcha Enferm, 30: 648-655.
7. Leão, S.C., J.F. de Araújo, A.R. Silveira, A.A.F. Queiroz and M.J.S. Souto *et al*., 2015. Management of exogenous intoxication by carbamates and organophosphates at an emergency unit. Rev. Assoc. Med. Bras., 61: 440-445.
8. Gunnell, D. and M. Eddleston, 2003. Suicide by intentional ingestion of pesticides: A continuing tragedy in developing countries. Int. J. Epidemiol., 32: 902-909.
9. Yao, B., Y. Li, R. Zhang, L. Yao, J. Xu, C. Yan and W. Chen, 2024. Simultaneous determination of 6 carbamate pesticides and relevant metabolites in oilseeds and oil with the modified fast QuECHERS method by ultra-performance liquid chromatography-tandem mass spectrometry. J. Future Foods, 4: 97-104.
10. Patel, S. and S. Sangeeta, 2019. Pesticides as the drivers of neuropsychotic diseases, cancers, and teratogenicity among agro-workers as well as general public. Environ. Sci. Pollut. Res., 26: 91-100.
11. Koffi, Y.S., J.H. Kouadio and D. Son, 2022. Pesticide exposure levels and risk assessment in operators involved in the cashew production in Côte d'Ivoire. Agric. Sci., 13: 86-104.
12. Mdeni, N.L., A.O. Adeniji, A.I. Okoh and O.O. Okoh, 2022. Analytical evaluation of carbamate and organophosphate pesticides in human and environmental matrices: A review. Molecules, Vol. 27. 10.3390/molecules27030618.
13. Alvarez, F., M. Arena, D. Auteri, M. Binaglia and A.F. Castoldi *et al*., 2022. Peer review of the pesticide risk assessment of the active substance oxamyl. Eur. Food Saf. Authority, Vol. 20. 10.2903/j.efsa.2022.7296.
14. Biancardi, A., C. Aimo, P. Piazza, F. Lo Chiano and S. Rubini *et al*., 2022. Acetylcholinesterase (AChE) reversible inhibitors: The role of oxamyl in the production of poisoned baits. Toxics, Vol. 10. 10.3390/toxics10080432.

15. OECD, 2002. OECD Guidelines for the Testing of Chemicals, Section 4 Test No. 423: Acute Oral toxicity-Acute Toxic Class Method. OECD Publishing, Berlin, Mexico, ISBN: 9789264071001, Pages: 14.
16. OECD, 2002. Test No. 404: Acute Dermal Irritation/Corrosion. OECD Publishing, Berlin, Mexico, ISBN: 9789264070622, Pages: 13.
17. Draize, J.H., G. Woodward and H.O. Calvery, 1944. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther., 82: 377-390.
18. Ouedraogo, G.G., I. Sawadogo, J.N.D. Kousse, S. Ilboudo and B. Tounkara *et al*., 2020. Assessment of oral toxicity, skin and eye irritation of *Cymbopogon nardus* (L.) Rendle (Poaceae) essential oil from Burkina Faso. Int. J. Adv. Res., 8: 1617-1626.
19. OECD, 2002. Test No. 405: Acute Eye Irritation/Corrosion. OECD Publishing, Berlin, Mexico, ISBN: 9789264070646, Pages: 21.
20. Wilhelmus, K.R., 2001. The draize eye test. Surv. Ophthalmol., 45: 493-515.
21. OECD, 2009. OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects Test No. 436: Acute Inhalation Toxicity-Acute Toxic Class Method. OECD Publishing, Berlin, Mexico, ISBN: 9789264076037, Pages: 27.
22. Artiss, J.D., M.W. McGowan, D.R. Strandbergh and B. Zak, 1982. A procedure for the kinetic colorimetric determination of serum cholinesterase activity. Clin. Chim. Acta, 124: 141-148.
23. Vale, A. and M. Lotti, 2015. Organophosphorus and Carbamate Insecticide Poisoning. In: Handbook of Clinical Neurology, Lotti, M. and M.L. Bleecker (Eds.), Elsevier, Amsterdam, Netherlands, ISBN: 9780444626271, pp: 149-168.
24. Silberman, J. and A. Taylor, 2023. Carbamate Toxicity. StatPearls Publishing, Treasure Island.
25. Kennedy Jr., G.L., 1986. Acute toxicity studies with oxamyl. Fundam. Appl. Toxicol., 6: 423-429.
26. Thabet, H., N. Brahmi, H. Elghord, N. Kouraichi and M. Amamou, 2013. Poisoning by Organophosphate and Carbamate Insecticides [In French]. In: Acute Poisonings, Baud, F., P. Hantson and H. Thabet (Eds.), Springer, Paris, France, ISBN: 978-2-8178-0300-5, pp: 281-296.